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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,505	08/29/2006	Manuel Ferrer	FERRER ET AL-1 PCT	3956
25889	7590	10/01/2009		
COLLARD & ROE, P.C. 1077 NORTHERN BOULEVARD ROSLYN, NY 11576			EXAMINER NASHED, NASHAAT T	
			ART UNIT	PAPER NUMBER
			1656	
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			10/01/2009	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/575,505	<b>Applicant(s)</b> FERRER ET AL.	
	<b>Examiner</b> NASHAAT T. NASHED	<b>Art Unit</b> 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 August 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 21-31 is/are pending in the application.
- 4a) Of the above claim(s) 27-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-26 and 31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/14/06 &amp; 3/18/08</u> .                                   | 6) <input type="checkbox"/> Other: _____                          |

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Applicant's election with traverse of Group III, claims 21-26 and 31, in the reply filed on August 27, 2009 is acknowledged. The traversal is on the ground(s) that: (a) Since the inventions of Group I-IV are linked by a single inventive concept, inventions (I) animal cells, plant cells (II), bacterial cell (III), or Fungal cell (IV) should be examined together; (b) the inventions of Groups I-IV and V-VIII should not be separated because the nucleic acid sequences and the cells were known separately; and (c) claims 27-30 of inventions IX-XII should not be separated from one another because they share a common inventive concept, i.e., cultivation at lower temperature. These are not found persuasive. The special technical features for inventions I-XII are the nucleic acid encoding the chaperonin of SEQ ID NO: 1 and 2 from *Oleispira Antartica*. The two sequences are distinct from one another and therefore, define two separate inventive concepts. Both sequences are previously known in the prior art, and thus, the inventive concepts are not the contribution of the applicants of the instant application. Thus, the restrictions between Groups I-IV, V-VIII, and IX-XII are proper. Since the claimed methods of Groups I-IV and V-VIII require both SEQ ID NO: 1 and 2, the restriction between inventions I-IV and V-VIII is hereby vacated. See IDS reference: Ranson *et al.* Biochem. J. 1998. With regard to the restriction between the various claimed cells, since the special technical concept is known in the prior art, different cells are distinct inventions and require separate searches in the patent and non-patent literature as evidenced by their separate classification, class/subclass: bacterial cells 435/252.3, animal cells 435/325, plant cells 435/410, fungi 435/254.1+. Thus, the restriction mailed July 27, 2009 is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 27-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 21-26 and 31 will be searched and examined to the extent of the elected subject matter, i.e., a process of utilizing a bacterial cell transformed with Cpn 60 and/or Cpn10 of SEQ ID NO's: 2 and 1, respectively.

Claims 21 and 23 are objected to because of the following informalities: (a) In claim 21, replace "Cpn60 and/or Cpn10 (Seq ID No. 1 and/or Seq ID No. 2)" with "Cpn60 of SEQ ID NO: 2 and/or Cpn10 of SEQ ID NO: 1", and replace "in using" by "using"; and (b) replace "Glu461 Ala" and "Ser471 Gly" with "Glu461Ala" and "Ser471Gly". Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 21, 22, 24-26, and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) The phrase “a functional mutant thereof” renders the claim indefinite because the resulting claim does not set forth the metes and bound of the desired patent protection. The specification does not define the phrase and one of ordinary skill in the art would not know what they are. For examination purposes only, the phrase interpreted as any protein having any sequence homology to SEQ ID NO: 1 and 2.

(b) The phrase “chaperonin” render the claim indefinite because the resulting claim does not set forth the metes and bound of the desired patent protection. The word “chaperonin” refers to the combination of both Cpn60 and Cpn10. See Ranson *et al.* page 234, right column, last three lines. The alternative statement which follows, i.e., Cpn60 and/orCpn10 negates the well accepted meaning of chaperonin. For examination purposes, the word is deleted from the claims.

(c) The phrase “fusion variants thereof” in claim 24 renders the claim indefinite because the resulting claim does not set forth the metes and bound of the desired patent protection. The phrase is not defined in the specification and one of ordinary skill in the art would not know the meaning of the phrase as it pertains to bacteria.

(d) Claims 22, 23, 25, 26, and 31 are included in this rejection because they are dependent on rejected claim and do not cure its deficiencies.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-26 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to the all possible host cells and nucleic acid sequences encoding any functional mutants of SEQ ID NO: 1 and 2 expressed in

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any host cell at a temperature below 25 degree C. Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses a method of utilizing any nucleic acid encoding any functional variant Cpn60 and/Cpn10 to express heterologous proteins in any host cell at a low temperature. That includes all possible nucleic acid sequences encoding all possible functional variants and mutants isolated from any biological or man-made DNA library. The specification provides guidance and examples in the form of an assay to isolate the nucleic acid encoding the polypeptide of SEQ ID NO: 1 and 2 from cold water bacteria *Oleispira antarctica*. See example 1 of the specification. Also, it teaches that the expression of said nucleic acid encoding SEQ ID NO: 1 and 2 in *E. coli* bacteria improve its growth at temperatures below 25 degrees C. In addition they teach the variants of SEQ ID NO: 2 that include stabilized mutant of SEQ ID NO: 6 and the destabilized mutant Lys468Thr/Ser471Gly and the expression of said mutants in *E. coli*. While molecular biological techniques and genetic manipulation to make the claimed constructs are known in the prior art and the skill of the artisan are well developed, knowledge regarding the nucleic acid encoding the functional variants of SEQ ID NO: 1 and 2, a host cell other than bacteria which can grow at a temperature below 25 degrees or 4-15 degrees when transferred with a nucleic acid encoding SEQ ID NO's: 1 and 2, and whether the expression of only one of the two proteins would be sufficient to enhance the growth rate of bacterial host cell at low temperature. It appears that the coexpression of the two proteins is required for their function. See IDS reference: Ranson *et al.* at page 234, right column, last paragraph. Thus, searching for nucleic acid encoding functional variants of SEQ ID NO: 1 and 2 to improve the growth of any mesophilic host cell at temperature below 25 degrees, is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation to identify a nucleic acid encoding a variant of SEQ ID NO: 1 or 2 capable of enhancing the growth of mesophilic host cell at a low temperature is enormous. Since routine experimentation in the art does not include screening vast numbers of genomic, cDNA or man-made nucleic acid libraries, identifying the coding sequence of functional variants of SEQ ID NO: 1 or 2, the appropriate host cell to express said variant, how to express one sequence and achieve the desired, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the biological source of the position of amino acid residues which can be deleted, substituted or inserted while maintaining the chaperonin activity, the host cells which can grow at lower temperature upon expressing

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SEQ ID NO: 1 and/or 2, or functional equivalent thereof, the three dimensional structure of the complex comprising SEQ ID NO 1 and 2. Without such guidance, the experimentation left to those skilled in the art is undue.

Claims 21-26 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to a method of expressing heterologous protein in any host cell in culture at a temperature below 25 degrees C by expressing Cpn60 and/or Cpn10 or functional equivalent thereof.

The court of Appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] name chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *UC California v. Eli Lilly* (43 USPQ2d 1398). For claims drawn to genus, MPEP section 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Also, MPEP section 2163 states that a representative number of species mean that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. At the time of invention, SEQ ID NO: 1 and 2 were known along with their function. See the search report. The specification describes two additional functional variants of SEQ ID NO: 2. While the enhanced growth of the host cell was demonstrated only in *E. coli*, no other host cell from any other higher organism is shown to have enhanced growth at lower temperature when SEQ ID NO: 1 and 2 are expressed. No host cell is shown that it has enhanced growth at lower temperature when either SEQ ID NO: 1 or 2 alone is expressed. Thus, the specification fails to describe additional representative species of these functional variant of SEQ ID NO: 1 or 2 and the enhance host cell growth at lower temperature of a host cells by any identifying structural characteristics or properties other than that it contains SEQ ID NO: 1 and 2 and the two variants of SEQ ID NO: 2 expressed in *E. coli* for which no predictability of structure to function is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

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No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NASHAAT T. NASHED whose telephone number is (571)272-0934. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nashaat T. Nashed/  
Primary Examiner, Art Unit 1656